

wards analysis unaccompanied by synthesis. Scientific men have mainly left it to philosophers and literary men to be the synthesizers of their data, shirking the task themselves with a few notable exceptions, of whom perhaps the greatest was a biologist, Charles Darwin. But analysis at best leads only to knowledge; while synthesis may furnish wisdom. And mankind sorely needs more wisdom right here and now!

PHARMACOLOGY.—*The toxicity for sheep of water solutions of hydrocyanic acid and the effectiveness of the nitrite-thiosulphate combination as a remedy.*<sup>1</sup> JAMES F. COUCH, A. B. CLAWSON and H. BUNYEA, Bureau of Animal Industry.

The results of a considerable number of experiments in which solutions of potassium cyanide were administered to sheep have previously been reported.<sup>2,3,4</sup> The potassium cyanide was administered as a drench and the quantity given in each case recorded as milligrams per kilogram of animal weight. In these experiments information was obtained concerning the smallest quantity of potassium cyanide that will produce symptoms in sheep, the smallest quantity that will kill and also concerning the effectiveness of a combination of sodium nitrite and sodium thiosulphate as a remedy for animals poisoned by potassium cyanide.

In the present paper data are presented concerning the toxicity for sheep of hydrocyanic acid in water solution and the remedial effectiveness of the nitrite-thiosulphate combination.

The solution of hydrocyanic acid used was prepared by mixing cold solutions of the calculated quantities of potassium cyanide and of tartaric acid in water and filtering off the precipitated potassium acid tartrate which was washed with a little cold water. The filtrate and washings were combined and diluted to a definite volume. The cyanide content of the solution was then determined by titration with N/10 silver nitrate solution and the strength was adjusted so that one cubic centimeter of solution contained 15.5 mg. of hydrocyanic acid. The solution contained less than 0.05 per cent of dissolved potassium acid tartrate which, in the doses given, was negligible.

A fresh solution was made each morning before experimental work, although analysis showed that there was no appreciable change in the strength of the solution when preserved for 72 hours in a cold place.

<sup>1</sup> Received February 28, 1935.

<sup>2</sup> This JOURNAL 24: 369-395. 1934.

<sup>3</sup> This JOURNAL 24: 528-532. 1934.

<sup>4</sup> This JOURNAL 25: 57-59. 1935.

TOXIC AND LETHAL QUANTITIES

In all, 29 experiments were made on 20 sheep. In 17 of these no remedies were administered, the experiments being made primarily to determine the effects of various quantities of hydrocyanic acid as compared with those produced by potassium cyanide. The general results obtained in the 17 cases are shown in table 1.

TABLE 1.—QUANTITIES OF HYDROCYANIC ACID GIVEN TO SHEEP AND THE EFFECTS PRODUCED WHEN NO REMEDIES WERE USED

Date 1935	Sheep		Quantities <sup>a</sup> given mg./kg. and effect			
	No.	Weight kg.	Symptoms	Sickness	Death	Remarks
Jan. 14	1451	34.47			3.38	
14	1462	38.55			3.10	
14	1460	41.72			2.75	
14	1461	43.54			2.74	
14	1463	38.55			2.65	
14	1459	43.99			2.64	
14	1465	33.11			2.63	
14	1452	49.89			2.55	
14	1458	41.72			2.41	
16	1456	35.37			2.32	
18	1474	37.64		2.31		A very poor sheep
14	1464	48.98			2.29	
14	1457	34.92	2.27			
14	1454	46.49		2.03		
14	1453	36.73		1.71		
14	1455	30.84	1.36			
14	1456	35.37	1.05			Very slight effect

<sup>a</sup> The quantities are given as milligrams of hydrocyanic acid per kilogram of animal weight.

The effects produced on sheep 1456 by 1.05 mg. per kg. of animal weight were so mild that the quantity for this animal was apparently very close to the minimum toxic dose. The fact that 2.29 mg. killed while 2.27 mg. produced only symptoms indicates that 2.29 mg. is the approximate minimum lethal dose for sheep. That 2.31 mg. did not kill sheep 1474, a very poor, underweight animal, is not considered as valid evidence against this conclusion. Were the dosage for this animal based on its normal weight when in good flesh, it would be much lower than the figure considered as the minimum lethal dose.

To compare, on a common basis, the toxicity of hydrocyanic acid with that of potassium cyanide, the dosages of the two substances may be reduced to the cyanide (CN) equivalents. On this basis the toxic and lethal doses of cyanide in the two forms are essentially the same.

Following the administration of hydrocyanic acid in 29 cases, symptoms appeared in from 20 seconds to 2 minutes, the average time being 50 seconds. The time to prostration or collapse varied more widely, it being 50 seconds in the shortest case and 51½ minutes in the longest. The longest period was with a sheep given slightly more than 1 m.l.d. Twenty-three cases had an average time of 5 minutes 52 seconds. In the average the animals given the larger quantities showed symptoms and collapsed in a shorter time than those given the smaller doses.

The average time to symptoms in the sheep given 3 to 4 lethal doses was 42 seconds; with those given 1 to 1.5 lethal quantities, it was 55 seconds; and with sheep given toxic but sub-lethal doses, 56 seconds.

The average period to collapse in those sheep given from 3 to 4 lethal quantities was 1 minute 31 seconds, while with those given less than 1.5 minimum lethal doses it was 9 minutes 13 seconds. The longer average was due in part, but not entirely, to the inclusion of two resistant and somewhat unusual cases.

Of the sheep which received no remedy, 11 died. The time between the drenching with cyanide and death varied between 12.5 minutes and 1 hour 22 minutes, and averaged 37 minutes 50 seconds.

#### RESULTS OF THE ADMINISTRATION OF THE REMEDY

To test the effectiveness of the nitrite-thiosulphate combination as a remedy in cases of poisoning by hydrocyanic acid, 12 experiments were made on 10 sheep. For experimental use a water solution containing 1 gram of sodium nitrite and 2 grams of sodium thiosulphate per 15 c.c. of solution was prepared. Based on 2.29 mg. per kg. as the minimum lethal dose, these animals were given doses of hydrocyanic acid ranging from 3 m.l.d. to 4.0 m.l.d. In periods varying from 0.8 to 4 minutes after being drenched with the cyanide they were then injected intraperitoneally with 15 c.c. of a solution of the nitrite-thiosulphate combination as a remedy.

The results of the administration of the nitrite-thiosulphate combination are shown in table 2.

In 10 cases the remedy was given after the animals had collapsed. Of these, six (or 60 per cent) recovered. One sheep was given the remedy as soon as symptoms were apparent and before collapse, and one was treated at the time of collapse. Both died.

TABLE 2.—SHOWING THE EFFECTS OF THE NITRITE-THIOSULPHATE COMBINATION ADMINISTERED INTRAPERITONEALLY AS A REMEDY FOR SHEEP POISONED BY HYDROCYANIC ACID

Date 1935	Sheep		Dose m.l.d.	Time from drench—			Effect
	No.	Weight kg.		To first symptom	To collapse	To giving remedy	
				Minutes			
Jan. 16	1457	34.92	3.	0.5	1.3	1.8	Recovery
14	1469	43.99	3.	1.0	1.5	2.	do
16	1470	43.54	3.	1.0	1.8	2.7	Death
17	1466	35.83	3.1	.5	1.3	1.75	do
17	1469	43.99	3.25	.8	1.5	2.5	Recovery
17	1473	40.82	3.25	.75	1.75	2.	Death
17	1457	34.92	3.25	.5	2.2	4.	Recovery
17	1453	36.73	3.50	.7	1.	1.5	do
17	1455	30.84	3.50	.7	1.75	2.	Death
17	1454	46.49	3.75	.75	2.	2.	do
17	1474	37.64	4.	.5	1.	1.5	Recovery
17	1475	40.82	4.	.8 ±	1.8	.8	Death

For the sake of comparison with the results obtained using the same remedy for sheep poisoned by potassium cyanide as given in a former paper,<sup>5</sup> table 3 is included. This is a summary of table 2. In it the doses of hydrocyanic acid are arranged in classes, and the number of survivals and deaths in each class shown.

TABLE 3.—EFFECTIVENESS OF THE REMEDY AGAINST VARYING QUANTITIES OF HYDROCYANIC ACID

Dose of HCN m.l.d.	Number of animals	Number that survived	Number that died	Per cent survived
3	4	2	2	50
3.25	3	2	1	67
3.5	2	1	1	50
3.75	1		1	0
4	2	1	1	50
Total	12	6	6	50

From table 3 it will be noted that the remedy was 50 per cent effective against as much as 4 minimum lethal doses of hydrocyanic acid. When compared with the results obtained with sheep poisoned by potassium cyanide, in which 2.75 m.l.d. was the largest dose against which protection was secured in 50 per cent or more of the cases,<sup>6</sup> it would appear that the remedy is more effective against poisoning by hydrocyanic acid itself than against poisoning by potassium cyanide.

<sup>5</sup> This JOURNAL 24: 369-395. 1934.

<sup>6</sup> This JOURNAL 24: 369-395. 1934.

## SUMMARY

When administered in sheep in a drench the minimum toxic dose of pure hydrocyanic acid is shown to be approximately 1.05 mg. per kg. of animal weight, and the minimum lethal dose is approximately 2.29 mg. per kg. When compared on a cyanide (CN) basis the differences in toxicity between hydrocyanic acid and potassium cyanide are slight and well within the limits of experimental error.

Following the administration of pure hydrocyanic acid, symptoms appear in an average of 50 seconds. The time to collapse is very variable. In the cases here reported the average time was 5 minutes 52 seconds. When no remedy was given the average time to death was nearly 38 minutes.

The nitrite-thiosulphate combination was 50 per cent effective as a remedy against from 3 to 4 m.l.d., and when injected intraperitoneally within 4 minutes after the hydrocyanic acid was administered.

GEOLOGY.—*Notes on the structure of the Erin shale of Alabama.*<sup>1</sup>

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## ABSTRACT

The Erin shale of east-central Alabama has previously been mapped as a stratigraphic unit in the Talladega slate. Fossils found in the Erin shale have been the basis for assigning a Carboniferous age to part or all of the Talladega slate and other crystalline rocks in the eastern part of the State. Evidence is presented to show that the contact between the Erin shale and the Talladega formation is a thrust fault dipping at a low angle eastward. The Erin shale is exposed by erosion through the overthrust block.

The type locality of the Erin shale of east-central Alabama is an area about 6 miles long and less than 1 mile wide. The exposure is in the valley of Talladega Creek along the east base of the Talladega Mountains in Clay County, Ala., about 8 miles northwest of Ashland. The Hillabee chlorite schist and the Ashland mica schist lie east of the Talladega formation (fig. 1). The Wedowee formation is east of the Ashland schist but is not shown on the map.

The Erin shale was described in 1903 by E. A. Smith, who considered it a lenticular mass in the Talladega slate, which he called "Ocoee."<sup>2</sup> Fossil plants were collected by Dr. Smith from the Erin shale and were determined by David White to be of Carboniferous age. Practically all papers treating of the Talladega slate that have appeared since 1903 have assigned a Carboniferous age to at least

<sup>1</sup> Published by permission of the Director, U. S. Geological Survey. Received March 30, 1935.

<sup>2</sup> SMITH, E. A. *Science*, new ser., 18: 244-246. 1903.